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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR     | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/919,345      | 07/30/2001  | Boris P. Belotserkovskii | A-69625-1/RFT/DLR   | 2746             |

7590 04/23/2003

FLEHR HOHBACH TEST  
ALBRITTON & HERBERT LLP  
Suite 3400  
Four Embarcadero Center  
San Francisco, CA 94111-4187

EXAMINER

LU, FRANK WEI MIN

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1634

DATE MAILED: 04/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/919,345

Applicant(s)

BELOTSEKOVSKII ET AL.

Examiner

Frank W Lu

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 13 January 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) 9-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 3-8 is/are rejected.
- 7) ☒ Claim(s) 2 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 8/1/2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☒ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 1/2002.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## Office Action Summary

Application No.

09/9/9345

Applicant(s)

Beldserkovskii, et al

Examiner

Lu, Frank

Group Art Unit

1634

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE \_\_\_\_\_ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

### Status

- ☐ Responsive to communication(s) filed on \_\_\_\_\_.
- ☐ This action is FINAL.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

### Disposition of Claims

- ☒ Claim(s) 1-35 is/are pending in the application.
- Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- ☒ Claim(s) 1-35 are subject to restriction or election requirement.

### Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
  - ☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been received.
  - ☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.
  - ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

### Attachment(s)

- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_
- ☐ Interview Summary, PTO-413
- ☐ Notice of Reference(s) Cited, PTO-892
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☒ Other Detailed Action

Office Action Summary

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICE

# EXAMINER'S CASE ACTION WORKSHEET

|                               |  |                           |
|-------------------------------|--|---------------------------|
| Application No.<br>09/919,345 |  | Legal Instrument Examiner |
|-------------------------------|--|---------------------------|

CHECK TYPE OF ACTION

DATE OF COUNT

|   |   |  |
|---|---|--|
| <input checked="" type="checkbox"/> Non-Final Rejection                                       | <input type="checkbox"/> Restriction/<br>Election Only  | <input type="checkbox"/> Final Rejection   |
| <input type="checkbox"/> Ex Parte Quayle  | <input type="checkbox"/> Allowance  | <input type="checkbox"/> Advisory Action   |
| <input type="checkbox"/> Examiner's Answer  | <input type="checkbox"/> Reply Brief Noted  | <input type="checkbox"/> Non-Entry of Late Paper   |
| <input type="checkbox"/> Defective Notice of Appeal or Defective Appeal Brief                 | <input type="checkbox"/> Interference SPE _____<br>(Approval for Disposal)                      | <input type="checkbox"/> Suspension SPE _____<br>(Initial)   |
| <input type="checkbox"/> Allowance After Examiner's Answer                                    | <input type="checkbox"/> SIR Disposal<br>(use only after FAOM)                                  | <input type="checkbox"/> Post-Allowance Communication  |
| <input type="checkbox"/> Miscellaneous Office Letter<br>(With Shortened Statutory Period Set) | <input type="checkbox"/> Notice of Non-Responsive Amendment<br>(With One Month Time Period set) | <input type="checkbox"/> Miscellaneous Office Letter<br>(No Response Period Set)                   |
| <input type="checkbox"/> Letter Requiring Formal Drawings                                     | <input type="checkbox"/> Supplemental Action<br>(Excluding Examiner's Answer)                   | <input type="checkbox"/> Response to a Rule 312 Amendment  |
| <input type="checkbox"/> Restart Time Period<br>(e.g., Missing References)                    | <input type="checkbox"/> Interview Summary  | <input type="checkbox"/> Authorization to Change Previous Office Action<br>SPE: _____<br>(Initial) |
| <input type="checkbox"/> Abandonment  | <input type="checkbox"/> Express Abandonment<br>Date: _____.                                    | <input type="checkbox"/> Abandonment After Examiner's Answer                                       |

Examiner's Name: Frank W Lu

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## **DETAILED ACTION**

### ***Election/Restriction***

1. Applicant's election of Group I, claim 1-11 and species I (claims 7 and 8 in Group I) in the response filed on January 13, 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Since species II, claims 9-11 are not elected by applicant, claims 1-8 will be examined.

### ***Priority***

2. The first sentence of the specification states "[T]his application is a continuing application of U.S.S.N. 60/222,272.". However, from the first sentence of the specification (see page 2 of the specification), it is unclear whether applicants claim priority for this provisional application or not. If applicants claim priority for this provisional application, applicants must specifically indicate in the first sentence of the specification that they claim benefits for a US provisional application 60/222,272.

### ***Information Disclosure Statement***

3. The examiner notes that some references such as O' Gorman et al., (1991), Science 251, 1351 in page 2, first paragraph of the specification are not in PTO 1449 form. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the

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Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

#### ***Oath/Declaration***

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: (1) it does not identify the citizenship of Boris Belotserkovskii, who is an inventor in this instant application; and (2) applicants change their filed No. without an initial (see page 2 of Oath/Declaration).

#### ***Specification***

5. The disclosure is objected to because of the following informalities: there are Figures 3C-1, 3C-2, 4A, and 4B in the drawings filed on January 8, 2002. However, the specification (see page 10) only describes Figures 3C and 4. Each figure, e.g., 3C-1 or 3C-2 or 4A or 4B, is considered to be a separate figure and needs to be described in the specification. Appropriate correction is required.

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***Sequence Rules Compliance***

6. The sequencing listing has complied with Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1 and 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Norden *et al.*, (The Journal of Biological Chemistry, 273, 15682-15686, June 1998).

The invention is drawn to a composition. Claim 1 requires a composition comprising an analog probe and a first single stranded nucleic acid probe that is coated with a recombinase wherein said analog probe and said first single stranded nucleic acid probe can be identical. In the specification, "analog probe" is defined as "nucleic acids containing modifications to the natural-occurring phosphodiester linkages or modifications to the natural occurring ribose backbone. In addition, analog probes hybridize to complementary nucleic acid sequences at least as well as the corresponding natural occurring nucleic acids.". Examples of analog probes include but are not limited to peptide nucleic acids (PNA), N3'-P5' phosphoramidate nucleic acids (NP), 2'- O-methoxyethyl nucleic acids and 2'-fluoro-arabino nucleic acids (see the specification, page 13, last paragraph bridging to page 14, first paragraph). Claim 6 requires that said first single

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stranded nucleic acid probe is DNA. Claims 7 and 8 further limit recombinase as recited in claim 1 as a prokaryotic recombinase such as RecA.

Norden *et al.*, teach base orientation of second DNA in RecA-DNA filaments. During the process of formation of RecA-DNA complex, a RecA-poly (dεA) complex was formed by mixing 50 μM RecA and 150 μM poly (dεA) (see page 15683, left column, third paragraph) wherein the Rec A was a protein that played a crucial role in homologous recombination in *Escherichia coli* and poly (dεA) was an etheno-modified DNA (see page 15682, abstract and left column).

Regarding claims 1 and 6-8, as shown above, a RecA-poly (dεA) complex was formed by mixing 50 μM RecA and 150 μM poly (dεA). Since initial concentration of poly (dεA)(150 μM) is three fold higher than that of RecA (50 μM), when binding of RecA to poly (dεA) reaches saturation, all of RecA is converted to the RecA-poly (dεA) complex if ratio of RecA to poly (dεA) in the RecA-poly (dεA) complex is 1:1 (RecA + poly (dεA)→RecA-poly (dεA)). In this situation, the concentration of free poly (dεA) in the solution is 100 μM after the binding is finished. Since RecA is a protein that plays a crucial role in homologous recombination in a prokaryotic cell (ie., *Escherichia coli*) and poly (dεA) is an etheno-modified DNA, the free poly (dεA) is an analog probe while poly (dεA) in the RecA-poly (dεA) complex is a first recombinase coated single stranded nucleic acid probe wherein the recombinase is prokaryotic recombinase (ie., RecA) as recited in claims 1 and 6-8.

Therefore, Norden *et al.*, teach all limitations recited in claims 1 and 6-8.



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***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1 and 3-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Norden *et al.*, (June 1998) in view of Faruqi *et al.*, (Proc. Natl. Acad. Sci. USA, 95, 1398-1403, February 1998).

Although the examiner indicates that the solution had free poly (dεA) after formation of RecA-poly (dεA) complex in above rejection under 35 U.S.C. 102, applicant may argue that Norden *et al.*, do not teach free poly (dεA) since Norden *et al.*, do not directly show that the solution had free poly (dεA) after formation of the RecA- poly (dεA) complex. Therefore, the

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examiner makes a following rejection under 35 U.S.C. 103(a) based on a totally different angle using a different part of the reference of Norden *et al.*.

The invention is drawn to a composition. Claim 1 requires a composition comprising an analog probe and a first single stranded nucleic acid probe that is coated with a recombinase. In the specification, "analog probe" is defined as "nucleic acids containing modifications to the natural-occurring phosphodiester linkages or modifications to the natural occurring ribose backbone. In addition, analog probes hybridize to complementary nucleic acid sequences at least as well as the corresponding natural occurring nucleic acids.". Examples of analog probes include but are not limited to peptide nucleic acids (PNA), N3'-P5' phosphoramidate nucleic acids (NP), 2'- O-methoxyethyl nucleic acids and 2'-fluoro-arabino nucleic acids (see the specification, page 13, last paragraph bridging to page 14, first paragraph). Claim 3 requires that analog probe recited in claim 1 comprises peptide nucleic acid. Claim 4 requires that analog probe recited in claim 1 is a fusion sequence comprising nucleoside analogs and naturally occurring nucleosides. Claim 5 requires that nucleoside analogs in claim 4 comprises at least one peptide nucleoside. Claim 6 requires that said first single stranded nucleic acid probe is DNA. Claims 7 and 8 further limit recombinase as recited in claim 1 as a prokaryotic recombinase such as RecA.

Norden *et al.*, teach base orientation of second DNA in RecA-DNA filaments. In another experiment, a RecA-poly (A) complex was first formed by mixing RecA and poly (A) and then a RecA-poly (A)-oligo(dT) complex was formed by adding oligo(dT) into the RecA-poly (A) complex in stoichiometric amounts (see page 15683, left column, third paragraph) wherein the Rec A was a protein that played a crucial role in homologous recombination in *Escherichia coli*

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(see page 15682, left column). Regarding claims 1 and 6-8, since Rec A is a protein that plays a crucial role in homologous recombination in a prokaryotic cell (ie., *Escherichia coli*), poly (A) and oligo (dT) are two nucleic acid probes in the RecA-poly (A)-oligo(dT) complex wherein poly (A) is a first recombinase coated single stranded nucleic acid probe and the recombinase is a prokaryotic recombinase (ie., RecA).

Norden *et al.*, do not disclose that the RecA-DNA triplex has an analog probe (ie., a peptide nucleic acid) as recited in claims 1 and 3-5.

Faruqi *et al.*, teach a peptide nucleic acid (PNA). PNA bound to DNA or RNA via Watson-Crick complementarity with binding affinity significantly higher than those of the corresponding DNA oligomers (see page 1398, left column, last paragraph) and PNA in a PNA-nucleic acid hybrid was resistant to both cellular nuclease and proteases (see 1398, right column, first paragraph). Regarding claims 1 and 3-5, according to the definition of "analog probe" (see above), PNA is an analog probe as recited in claims 1 and 3. Since a PNA probe, PN-10, in Table 1 (see page 1399, left column) has nucleoside analogs (ie., J or C-Lys-Lys-Lys) and naturally occurring nucleosides (ie., T), PN-10 is an analog probe with a fusion sequence comprising nucleoside analogs and naturally occurring nucleosides as recited in claim 4. Since PN-10 has one peptide nucleoside (ie., C-Lys-Lys-Lys), nucleotide analog in PN-10 comprises at least one peptide nucleoside as recited in claim 5.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made a composition comprising an analog probe (ie., PNA) and a first single stranded nucleic acid probe that is coated with a recombinase (ie., RecA)

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in view of the prior art of Norden *et al.*, and Faruqi *et al.*. One having ordinary skill in the art would have been motivated to do so because Faruqi *et al.*, have shown that a PNA-DNA hybrid was more stable than a hybrid formed by DNAs since binding affinity of PNA to a DNA is significantly higher than those of the corresponding DNA oligomers (see Faruqi *et al.*, page 1398, left column, last paragraph) and PNA in a PNA-DNA hybrid is resistant to both cellular nuclease and proteases, and the simple replacement of a regular nucleic acid with a modified nucleic acid (i.e., a PNA) during the process of making a composition as recited in claims 1 and 3 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because the replacement of oligo (dT) in RecA-poly(A)-oligo (dT) complex taught by Faruqi *et al.*, by its corresponding PNA would generate a more stable nucleic acid hybrid

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements in such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

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***Conclusion***


10. Claim 2 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims since Norden *et al.*, do not teach a second single stranded nucleic acid probe that is coated with a recombinase and is substantially complementary to said first probe.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119.

Any inquiry of a general nature or relating to the status of this application should be directed to the patent Analyst of the Art Unit, Ms. Chantae Dessau, whose telephone number is (703) 605-1237.

  
Frank Lu  
April 17, 2003